ABSORBABLE BIOMATERIAL AND ITS PRODUCTION

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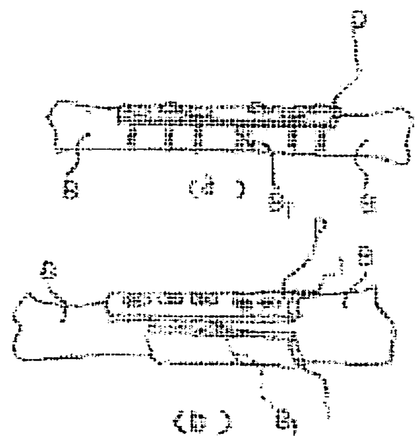
Abstract of **JP 7116241 (A)**

PURPOSE:To provide the absorbable biomaterial which is safe in a living body, accelerates formation of capillary vessels and is capable of restoring packed points with natural bones by producing the absorbable biomaterial of thermally cross-linked chitin or its deriv. and forming the material in such a manner that the material has a density to exhibit an adequate degradation and absorption rate in the living body. CONSTITUTION:This absorbable biomaterial is formed by fixing the fractured bone B with a plate P for fixing, then thermally cross-linked chitin or its deriv.; The absorbable biomaterial 1 which has about a thickness of 10 to 1000mum and average grain size of 5 to 100mum and is porous and single layer film form is stuck by using an extremely slight amt. of an instant set adhesive to the entire circumference (exclusive of the point of the plate P) of the bone fracture point B1. The absorbable biomaterial 1 consists of the thermally cross-linked chitin or its deriv. and has a density of 0.07 to 0.7g/cm<3>. The absorbable biomaterial is produced by the process of freeze-drying a soln. of the chitin or its deriv. and air drying the freeze-dried chitin or its deriv., then thermally cross-linking the chitin or its deriv. in a vacuum. The soln. of the chitin or its deriv. is otherwise freeze-dried and thereafter, the soln. is applied on the separately freeze-dried chitin or its deriv.



CLAIMS

[Claim(s)]
[Claim 1]A resorbable biomaterial which consists of a kitchen which carried out heat bridge construction, or its derivative.
[Claim 2]A resorbable biomaterial consisting of a kitchen which carried out heat bridge construction, or its derivative, and having the density of 0.07-0.7g / cm^3.
[Claim 3]A manufacturing method of a resorbable biomaterial characterized by carrying out heat bridge construction in a vacuum after freeze-drying a solution of a kitchen or its derivative and air-drying this.
[Claim 4]A manufacturing method of a charge of absorptivity living body material of claim 2 applying on a kitchen which freeze-dried this solution separately, or its derivative after freeze-drying a solution of a kitchen or its derivative.

[Translation done.]

DETAILED DESCRIPTION

[Detailed Description of the Invention]
[0001]
[Industrial Application]This invention consists of material obtained from natural organisms, such as collagen and a kitchen, and relates to the biomechanical material used for surgical treatment, such as a bone deficit, damage, and an odontectomy, and an orthopedics operation.
[0002]
[Description of the Prior Art]The biomechanical material which consists of material obtained from living thing organizations, such as collagen and a kitchen, conventionally was filled up with block like shape in a bone deficit, an injured spot, and the odontectomy socket etc., it used in order to patch up the part and to maintain a gestalt, or the wound as film-like covering material was blocked, and it has been used in order to prevent infection etc.
[0003]Among such biomechanical materials, as a filler of block like shape, the porosity sponge of an invention of JP,62-39506,A constructs a bridge in a kitchen with drugs, and is unabsorbent in the living body, for example.
It excels in firmness.

[0004]The composite material of an invention of JP,3-23864,A is used as a filler of block like shape, and this composite material consists of collagen sponge and polylactic acid, and is absorptivity in the living body.
[0005]As the above-mentioned wound covering material, the charge of a laminated material of an invention of JP,2-268766,A is wound covering material of the shape of a NI layer membrane of the porosity which constructs a bridge with drugs in chitosan, and nonporosity, and in order to prevent infection, the outside is a nature film of nonporous, for example.
In order to stick with an another side wound, the inside serves as a porous membrane.

[0006]
[Description of the Prior Art]However, there were the following technical problems in the above-mentioned conventional technology. Namely, since it is the fault that tissue may invade into a lacking part and bony generation is overdue, and unabsorbent and it is not thoroughly replaced by the bone itself in order that the above-mentioned porosity sponge may suture tissue and may carry out an affected part blockade after filling up a lacking part, There is a danger that the danger and the material itself of infection will break away, and the; above-mentioned composite material has some antigenicity in atelocollagen, and there is fault of triggering the inflammatory reaction of a body tissue at the time of disassembly of polylactic acid and absorption, and, as for the charge of the; above-mentioned laminated material, the nature film of nonporous prevents a bacterial invasion.
The fault that on the other hand it is inapplicable to the insides of a living body (the inside of the mouth, a bone lacking part, etc.) since the tissue fluid containing a nutrient etc. is not circulated in and abroad, Since fault that processes, such as the dissolution, coagulation, and neutralization, are complicated in the process, and drugs processing were performed, there was a possibility that it might have an adverse effect to a living body with processing drugs.

[0007]
[Means for Solving the Problem]In order to solve an aforementioned problem, this invention provides a resorbable biomaterial with density which consists of a kitchen which carried out heat bridge construction,

or its derivative, and shows a moderate decomposition rate of absorption in the living body.
[0008]In order to obtain such a material, performing vacuum heat crosslinking treatment and press forming provides a manufacturing method of the main feature slack resorbable biomaterial.
[0009]
[Example]Hereafter, the example of this invention is described. Put in the solution of a kitchen or its derivative in containers, such as a cylindrical shape container and Chalais, and it freeze-dries, After performing press forming to this if needed and being air-dry at the temperature of 30 degrees or less, a resorbable biomaterial is preferably manufactured at the process which is heated in a vacuum with a bridge construction temperature of 120 degrees - 180 degrees for about 24 hours and which carries out heat bridge construction.
[0010]Thus, since the biomechanical material manufactured is manufactured without using the kitchen excellent in biocompatibility, or its derivative as a raw material, and using the drugs for bridge construction, while it is safe in the living body, By having carried out heat bridge construction in the vacuum, it decomposes temporally in the living body, and if this decomposed kitchen or its derivative promotes capillary generation and fills up a bone lacking part, odontectomy socket, etc. as block like shape by this, it has the character in which a restoration part restores thoroughly by a natural bone.
[0011]This biomechanical material can be manufactured above comparatively easily, by extending thinly and, for example, making it freeze-dry in Chalais besides as a charge of living body material of block like shape, can obtain a film-like biomechanical material and covers a bone lacking part, odontectomy socket, etc. using this.
[0012]The biomechanical material of the shape of this 1 layer membrane can control thickness, an average pore size, and density suitably by adjusting the concentration of a solution, etc. or applying compression molding if needed after freeze-drying. By controlling them, although the tissue fluid containing a nutrient is circulated, it makes and, thereby, a required period and the perfect bone repair by a natural bone can do environment which promotes the bone formation of tissue not making it invade.
[0013]By adding the work which applies the above-mentioned solution after freeze-drying, It is formed without passing through freeze-drying, can obtain the biomechanical material of the shape of a bilayer film which added the film which has a bigger average pore size to the 1 layer-membrane biomechanical material of the above, and the biomechanical material of the shape of this bilayer film, By controlling suitably the membranous thickness and average pore size which are added so that marrow cells and various cells may adsorb, and using this as said covering material, bone formation active in the surface part of this film starts, and also the environment which a bone tends to generate can be provided.
[0014]Furthermore, the biomechanical material according [the result of research] to a heat bridge construction temperature lower than 120 degreeC carried out the knowledge of what a mechanical strength is small and depends on a heat bridge construction temperature higher than 180 degrees of another side C having a small mechanical strength while the dissolution rate might dissolve that bone formation became active early, without waiting.
[0015]Since said biomechanical material which consists of a kitchen which carried out heat bridge construction, or its derivative has high absorptivity and no bridge construction drugs are used, anythings other than a kitchen or its derivative are not detected except the substance mixed unescapable. On the other hand, while the biomechanical material of the kitchen which constructed the bridge with drugs, or its derivative has low absorptivity and being unabsorbent in the living body, when it analyzes by the chemical method etc., bridge construction drugs are detected.
[0016]Next, a figure explains the example of use of said biomechanical material in detail. After fixing the bone B broken as drawing 1 showed 1 condition of use of a biomechanical material and it was shown in the figure (a) on the plate P for immobilization, As shown in (b), heat bridge construction of a kitchen or its derivative was carried out, by 10-1000 micrometers in thickness, and 5-1000 micrometers of average pore sizes, the moment binder of ultralow volume was used for the perimeter enclosure (except for the part of the plate P) of fracture part B_1, and the biomechanical material 1 of porous state and the shape of 1 layer membrane was stuck on it.
[0017]Such a biomechanical material 1 had the following operations. That is, since the biomechanical material 1 provided the environment which promotes bone formation good, without tissue's not having made it invade but hyperostosis being checked by tissue by this, although the tissue fluid which contains a nutrient to fracture part B_1 was circulated by the above-mentioned thickness and an average pore size, early and precise bone formation realized it. Since the above-mentioned biomechanical material 1 is what carries out heat bridge construction of a kitchen or its derivative without using drugs, while having

biocompatibility, it is safe, and since it dissolves slowly further in the living body, it decomposes, and after affected part recovery is absorbed by the inside of the body, and does not need to take this out by operation etc.

[0018]Another condition of use of the above-mentioned biomechanical material 1 was shown in drawing 2, the gum S was cleared, and further, deficit opening D_1 of the alveolar bone D under it was covered as the film-like biomechanical material 1 is also. By doing in this way, the environment which promotes bone formation good as mentioned above was provided, and the therapy of bone deficit opening D_1 by early and precise bone formation was completed.

[0019]Another condition of use of the above-mentioned biomechanical material 1 was shown in drawing 3 thru/or drawing 4, bone deficit opening B_2 of the bone B was filled up with private spicule B_3 in both figures, and this bone deficit opening B_2 was covered with the charge 1 of living body material.

[0020]Heat bridge construction of a kitchen or its derivative may be carried out in order to fill the residual opening with private spicule B_3 to bone deficit opening B_2, as shown in drawing 4, and it may be filled up with the biomechanical material 2 of the porosity of 10-1000 micrometers of average pore sizes, and block like shape. Capillary generation is promoted and both the biomechanical materials 2 of such block like shape make the decomposed part carry out hyperplasia of the bone at an early stage, when decomposed in the living body when it comes to the scaffold of bone formation. Thereby, a restoration part can restore thoroughly by a natural bone, and since it prevents that private spicule B_3 rocks simultaneously with it, the therapy of bone deficit opening B_2 by early and precise bone formation can be performed.

[0021]Another operating mode used combining the film-like biomechanical material 1 and the biomechanical material 2 of block like shape like drawing 4 is shown in drawing 5, After pulling out the biomechanical material 2 of block like shape was filled [deficit opening D_2 / whole] up via the gum S cleared as shown in the figure, and this deficit opening D_2 was further covered with the film-like biomechanical material 1.

[0022]. Next, made into one two films of the porosity description which has an average pore size which carries out heat bridge construction of a kitchen or its derivative, and is different in drawing 6. Bilayer film-like the biomechanical material 3 and 1 condition of use are shown, and this biomechanical material 3, The porous thick film 3b carries out confrontation adherence in the one direction of the porous thin film 3a by 300-1000 micrometers in thickness, and 50-500 micrometers of average pore sizes by the same description of 20-100 micrometers as the biomechanical material 1 of the shape of said 1 layer membrane, i.e., thickness, and 2-20 micrometers of average pore sizes.

[0023]By the gum S cut open as an example of the condition of use to the part to which the alveolar bone D suffered a loss in part as shown in drawing 6. After embedding the fixture F of a dental implant in the alveolar bone which remains, as the gum S was met in the above-mentioned thin film 3a and the alveolar bone D was met in the thick film 3b, respectively, deficit opening D_1 was covered as the biomechanical material 3 of the shape of said bilayer film is also.

[0024]The biomechanical material 3 of the shape of such a bilayer film has the following operations. Namely, the above-mentioned thin film 3a receives the above-mentioned deficit opening D_1 like the biomechanical material 1 of the shape of said 1 layer membrane, While providing the environment which promotes bone formation good, without tissue's not invading but having bone formation checked by tissue by this, although the tissue fluid which contains a nutrient through the above-mentioned thick film 3b is circulated, the thick film 3b -- that thickness and average pore size -- marrow cells and various cells -- that hole -- it is easy to adsorb inside, therefore easy to generate a new bone into this portion.

[0025]As shown in drawing 6, it can be filled up with the biomechanical material 2 of said block like shape in the above-mentioned deficit opening D_1, and this can be used together.

[0026]The following thing became clear. [A]In the thin film 3a of the 1 layer-membrane biomechanical material 1 of the above, and the bilayer film-like biomechanical material 3, Thickness is larger than 1000 micrometers, or - Or when an average pore size is smaller than 10 micrometers, Since circulation of tissue fluid becomes inactive, a mechanical strength becomes small when - thickness is smaller than 10 micrometers, and tissue is circulated when - average pore size is larger than 1000 micrometers, it is desirable that they are 10-1000 micrometers of thickness and 5-1000 micrometers of average pore sizes.

[0027][B]When - average pore size is 10-1000 micrometers in the thickness 3b of the bilayer film biomechanical material 3 of the above, When marrow cells and various cells tend to adsorb in a hole and -

average pore size is smaller than 10 micrometers, Or when thickness is smaller than 50 micrometers, there is little amount of adsorption of marrow cells and various cells, - When an average pore size is larger than *1000* micrometers, thru/or when thickness is larger than 5000 micrometers, since a mechanical strength becomes small, it is desirable that they are 50-5000 micrometers of thickness and 10-1000 micrometers of average pore sizes.
[0028]Although this example showed the example which is independent, or combined and used the biomechanical materials 1, 2, and 3 of the shape of a film, block like shape, and the shape of a bilayer film further, This invention is not limited to such descriptions and combination, and is doubled with the state of the affected part, The biomechanical material which carries out heat bridge construction of a kitchen or its derivative in order to provide the optimal environment for bone formation is formed in the optimal description, And it can use with the combination of the optimal description, and since it dissolves slowly in the living body even if it is which description, it decomposes, and after affected part recovery is absorbed by the inside of the body, and does not need to take this out by operation etc.
[0029]It is preferred that they are 0.07-0.7g / cm^3 as density of a biomechanical material. There is a possibility of disappearing before affected part recovery since the mechanical strength of a biomechanical material is small and the rate of absorption is too early when density is lower than 0.07g / cm^3, If it is going to make density larger than 0.7 and the quantity of a kitchen or its derivative is increased, in order will be saturated to water and to melt thoroughly, there is fault that drugs must be used. When the above-mentioned densities were 0.2-0.6g / cm^3 wholeheartedly as a result of examination, it turned out that it becomes the thing stable also in mechanical strength, and will become still more desirable.
[0030]In one or less-example order, the carboxylmethyl kitchen (it is considered as CM kitchen below) powder of 60% of the degree of formation of :** carboxylmethyl which created the biomechanical material 1 of the shape of said 1 layer membrane was dissolved in distilled water, and 3.0wt% solution was adjusted.
** To six phi10cm glass SHARE, it poured in and spread 20g of the above-mentioned solution at a time.
** Above-mentioned glass SHARE was quick-frozen at -20 **, and it freeze-dried.
** CM kitchen object taken out from glass SHARE was air-dried at the temperature of 30 ** or less.
[0031]** It gave at the temperature of 120 **, 140 **, 160 **, and 180 **, and heat crosslinking treatment was performed to the above-mentioned CM kitchen object in the vacuum for 24 hours.
[0032]The thickness and the average pore size of each biomechanical material 1 were as being shown in Table 1.
[0033]
[Table 1]

熱架橋温度（℃）	膜厚（μm）	平均孔径（μm）
120	60	40
140	50	40
160	45	35
180	45	35

[0034]CM chitin powder of 60% of the degree of formation of example 2 carboxylmethyl is dissolved in distilled water, 10. The 0wt% solution 20g was adjusted, and it poured into two metallic molds (un-illustrating) which have the inner shape of the shape of a cube length, width, and whose height are 1.0cmx1.0cmx1.0cm about this solution, respectively, and freeze-dried by quick-freezing at -20 **. Press forming was performed only to one side of these CM kitchen objects, it presupposed that it is like an abbreviation half about thickness, these were taken out from the metallic mold, and it was air-dry at the temperature of 30 degrees or less. And when it gave at 140 ** and heat crosslinking treatment was performed to CM kitchen object in the vacuum for 24 hours, the biomechanical material (100 micrometers

and 200 micrometers) was obtained for thickness, respectively.

[0035]The densities of these absorbent materials were 0.0352g / 0.2 cm^3->about 0.176g /, cm^3, and 0.0352g / 0.1 cm^3->about 0.352g / and cm^3.

[0036]1.0 g of kitchens which 350% of the example deacetylated were dissolved in distilled water, 1.0wt% of solution was adjusted, and others are the same methods as Example 1, and produced the charge 1 of living body material of the shape of said 1 layer membrane. As a result, it observed that an average pore size became large somewhat from the biomechanical material 1 of Example 1.

[0037]As shown in example 4 drawing 7, the container 10 provided with the lid 12 for extrusion which equipped the lower end of the main part 11 of the shape of a phi5mm cylinder with the handle 12a, and the top cover 13 which equipped the upper bed with the vent 13a is used, The biomechanical material 2 of the block like shape which carried out phi1.6-1.8mm cylindrical shape according to the method of Example 1 was produced. The thickness and the average pore size of each biomechanical material 2 were as being shown in Table 2.

[0038]

[Table 2]

熱架橋温度 (℃)	平均孔径 (μm)
120	20
140	15
160	15
180	15

[0039]Said biomechanical material 3 was produced for CM kitchen solution by the same method as Example 1 after example 5 freeze-drying except [of CM kitchen object] on the other hand applying to a field. The thickness and the average pore size of said thin film 3a and the thick film 3b in each biomechanical material 3 were as being shown in Table 3.

[0040]

[Table 3]

熱架橋温度	膜厚 (μm)		平均孔径 (μm)	
	薄膜3a	厚膜3b	薄膜3a	厚膜3b
120	40	800	30	80
140	35	750	20	70
160	35	730	20	70
180	76	720	20	60

[0041]The NZW rabbit which provided the breeding period for one week in before an operation as shown in animal experiment 1 drawing 8 : Cylindrical bone deficit B_4 (phi2.0mm) is formed in the bone B of the 12-week old facies medialis tibiae, The above-mentioned bone deficit B_4 was covered at the moment with the

biomechanical material 3 which is the biomechanical material 3 of the shape of a bilayer film which removed the periosteum after pressure and hemostasis and was produced in Example 5, and carried out trimming of the bleeding from this bone deficit B_4 to the size of 5x5 mm beforehand, using a binder for a very small quantity very much, and muscles and the skin were sutured promptly after this.
[0042]slaughtering the above-mentioned NZW rabbit after the operation and in four weeks, and extracting a tibia part -- a connoisseur -- the deliming specimen was produced in accordance with the method. Dyeing performed H-E dyeing and PAS stain, and performed observation by an optical microscope.
[0043]The result checks that the new bone conglutinated in the center and the above-mentioned bone deficit B_4 has been blocked at the outside-surface side as shown in the mimetic diagram of the preparation image of drawing 10, Among these, a new bone fills bone deficit B_4 with the specimen by the bridge construction temperature of 140 **, and the 160 ** biomechanical material 3 mostly.
[0044]From bone deficit B_4 formed [as well as the animal experiment double thing experiment 1] and adjusted, it was filled up as the biomechanical material 2 of the block like shape produced in Example 4 was shown in drawing 9, and the preparation was produced and observed in the similar way.
[0045]Also in this experiment, new bone B_5 was generating most densely by the specimen by the heat bridge construction temperature of 140 **, and the 160 ** biomechanical material 2. However, on the whole, it said and generation of the new bone was more precise than the specimen of this experiment of the way of the specimen of the animal experiment 1.
[0046]
[Effect of the Invention]Like the above statement, the biomechanical material of this invention is an absorbent material of the porosity decomposed in the living body, when it excels in compatibility with a living body and bone formation occurs enough.
** When it uses as film-like covering material further, by controlling an average pore size suitably, When the environment which promotes bone formation could be provided and it uses as a filler of ** block like shape, By a natural bone, can restore a restoration part thoroughly and **** further on film-like covering material, By forming the porous membrane which controlled thickness and an average pore size suitably, and using as bilayer film-like covering material, ** which provides the environment a bone is further apt to generate is made so that marrow cells and various cells may adsorb.
A safe absorbent material can be manufactured in the living body by carrying out heat crosslinking treatment of the biomechanical material which consists of a kitchen or its derivative.

[Translation done.]